Chernyshev
09/267511

FILE 'REGISTRY' ENTERED AT 10:29:10 ON 24 FEB 2005
L1 63 SEA ABB=ON PLU=ON SALLRSIPA|NAPVSIPQ/SQSP

FILE 'CAPLUS' ENTERED AT 10:29:25 ON 24 FEB 2005
L2 63 SEA ABB=ON PLU=ON L1
L3 24 SEA ABB=ON PLU=ON L2 AND ((FET## OR FOET##)(W)(ALC OR ALCOHOL)(W)SYNDROM? OR FAS(S)SYNDROM? OR (NEURON? OR NERV###)(5A)(CELL DEATH OR APOPTOSIS OR APOPTOT?))

L3 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 22 Nov 2004
ACCESSION NUMBER: 2004:1001032 CAPLUS
DOCUMENT NUMBER: 142:17815
TITLE: Neuroprotective effect of activity-dependent neurotrophic factor against toxicity from familial amyotrophic lateral sclerosis-linked mutant SOD1 in vitro and in vivo
AUTHOR(S): Chiba, Tomohiro; Hashimoto, Yuichi; Tajima, Hirohisa; Yamada, Marina; Kato, Rikiya; Niikura, Takako; Terashita, Kenzo; Schulman, Howard; Aiso, Sadakazu; Kita, Yoshiko; Matsuoka, Masaaki; Nishimoto, Ikuo
CORPORATE SOURCE: Department of Pharmacology, KEIO University School of Medicine, Tokyo, Japan
SOURCE: Journal of Neuroscience Research (2004), 78(4), 542-552
CODEN: JNREDK; ISSN: 0360-4012
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Amyotrophic lateral sclerosis (ALS) is the most common fatal motor neuron disease, affecting mostly middle-aged people. There are no curative therapies for ALS. Several lines of evidence have supported the notion that the proapoptotic property of familial ALS (FALS)-linked mutant Cu/Zn-superoxide dismutase-1 (SOD1) genes may play an important role in the pathogenesis of some FALS cases. Here we found that activity-dependent neurotrophic factor (ADNF), a neurotrophic factor originally identified to have the anti-Alzheimer's disease (AD) activity, protected against **neuronal cell death** caused by FALS-linked A4T-, G85R- and G93R-SOD1 in a dose-responsive fashion. Notably, ADNF-mediated complete suppression of SOD1 mutant-induced **neuronal cell death** occurs at concns. as low as 100 fM. ADNF maintains the neuroprotective activity even at concns. of more than 1 nM. This is in clear contrast to the previous finding that ADNF loses its protective activity against neurotoxicity induced by AD-relevant insults, including some familial AD genes and amyloid β peptide at concns. of more than 1 nM. Characterization of the neuroprotective activity of ADNF against cell death caused by SOD1 mutants revealed that CaMKIV and certain tyrosine kinases are involved in ADNF-mediated neuroprotection. Moreover, in vivo studies showed that intracerebroventricularly administered ADNF significantly improved motor performance of G93A-SOD1 transgenic mice, a widely used model of FALS, although survival was extended only marginally. Thus, the neuroprotective activity of ADNF provides a novel insight into the development of curative drugs for ALS.
IT **177718-96-6**, Activity-dependent neurotropic factor peptide-9
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action);

PAC (Pharmacological activity); BIOL (Biological study)
(activity-dependent neurotrophic factor neuroprotective effect against toxicity from familial amyotrophic lateral sclerosis-linked mutant SOD1 in vitro and in vivo)
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 07 Jun 2004
ACCESSION NUMBER: 2004:454464 CAPLUS
DOCUMENT NUMBER: 141:64409
TITLE: Protective peptides that are orally active and mechanistically nonchiral
AUTHOR(S): Brenneman, Douglas E.; Spong, Catherine Y.; Hauser, Janet M.; Abebe, Daniel; Pinhasov, Albert; Golian, Tania; Gozes, Illana
CORPORATE SOURCE: Section on Developmental and Molecular Pharmacology, Laboratory of Developmental Neurobiology, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 309(3), 1190-1197
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous reports identified two peptides that mimic the action of neuroprotective proteins derived from astrocytes. These peptides, NAPVSIPQ and SALLRSIPA, prevent **neuronal cell death** produced by elec. blockade, N-methyl-D-aspartate, and β-amyloid peptide (25-35). In the present study, all D-amino acid peptides of NAPVSIPQ and SALLRSIPA were synthesized and compared resp. to the corresponding all L-amino acid peptides. In rat cerebral cortical test cultures cotreated with 1 μM tetrodotoxin, the D-amino acid peptides produced similar potency and efficacy for neuroprotection as that observed for their resp. L-amino acid peptides. Since all these peptides tested individually exhibited attenuation of efficacy at concns. of > 10 pM, combinations of these peptides were tested for possible synergies. Equimolar D-NAPVSIPQ and D-SALLRSIPA combination treatment produced potent neuroprotection (EC50, 0.03 fM) that did not attenuate with increasing concns. Similarly, the combination ofL-NAPVSIPQ and D-SALLRSIPA also had high potency (EC50, 0.07 fM) without attenuation of efficacy. Combined administration of peptides was tested in a model of **fetal alc. syndrome** and in a model of learning impairment: apolipoprotein E knockout mice. I.p. administration of D-NAPVSIPQ plus D-SALLRSIPA to pregnant mice (embryonic day 8) attenuated fetal demise after treatment with an acute high dose of alc. Furthermore, oral administration of D-NAPVSIPQ plus D-SALLRSIPA significantly increased fetal survival after maternal alc. treatment. Apolipoprotein E knockout mice injected with D-NAPVSIPQ plus D-SALLRSIPA showed improved performance in the Morris water maze. These studies suggest therapeutic potential for the combined administration of neuroprotective peptides that can act through a mechanism independent of chiral recognition.

IT **177718-96-6 211439-12-2**, NAPVSIPQ **327157-61-9 327157-62-0**

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protective peptides that are orally active and mechanistically nonchiral)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 07 Jun 2004
ACCESSION NUMBER: 2004:454463 CAPLUS
DOCUMENT NUMBER: 141:201591
TITLE: Ethanol antagonist peptides: Structural specificity without stereospecificity
AUTHOR(S): Wilkemeyer, Michael F.; Chen, Shao-yu; Menkari, Carrie E.; Sulik, Kathleen K.; Charness, Michael E.
CORPORATE SOURCE: Neurology Service, Veterans Affairs Boston Healthcare System, MA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 309(3), 1183-1189
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Increasing evidence suggests that ethanol damages the developing nervous system partly by disrupting the L1 cell adhesion mol. Ethanol inhibits L1-mediated cell adhesion, and compds. that antagonize this action also prevent ethanol-induced embryotoxicity. Two such compds. are the small peptides NAPVSIPQ (NAP) and SALLRSIPA (SAL). The authors showed previously that NAP and SAL antagonize ethanol inhibition of L1 adhesion at femtomolar to picomolar concns. Here the authors show that, despite this extraordinary potency, both NAP and SAL lack stereospecificity. D-NAP, a peptide composed entirely of D-amino acids, was an effective ethanol antagonist in NIH/3T3 cells transfected with human L1 and in the NG108-15 neural cell line. Interestingly, Ala-substituted derivs. of D-NAP demonstrate the same structure-activity relation as the corresponding derivs. of L-NAP. The Ser-Ile-Pro motif was important for the ethanol antagonist activity of D-NAP, L-NAP, and L-SAL, with Ile being the most critical element in all three. Like L-NAP, D-NAP effectively reduced ethanol-induced growth retardation in mouse whole embryo culture. The potential resistance of D-peptides to proteases makes D-NAP a potentially attractive agent for the prevention of **fetal alc. syndrome.**
IT **177718-96-6 211439-12-2**, NAPVSIPQ **327157-61-9 327157-62-0**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(ethanol antagonist peptides are structurally specific but not stereospecific)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 08 Oct 2003
ACCESSION NUMBER: 2003:786849 CAPLUS
DOCUMENT NUMBER: 140:37325
TITLE: The role of activity-dependent neuroprotective protein

in a mouse model of **fetal alcohol syndrome**

AUTHOR(S): Poggi, Sarah H.; Goodwin, Katie; Hill, Joanna M.; Brenneman, Douglas E.; Tendi, Elizabetta; Schinelli, Sergio; Abebe, Daniel; Spong, Catherine Y.

CORPORATE SOURCE: Department of Obstetrics and Gynecology, Georgetown Univ. Hosp., National Institutes of Health, Bethesda, DC, USA

SOURCE: American Journal of Obstetrics and Gynecology (2003), 189(3), 790-793
CODEN: AJOGAH; ISSN: 0002-9378

PUBLISHER: Mosby, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Objective: **Fetal alc. syndrome** (**FAS**) is the most common nongenetic cause of mental retardation. Peptides NAPVSIPQ (NAP) and SALLRSIPA (SAL), related to activity-dependent neuroprotective protein (ADNP), prevent alc.-induced damage in a mouse model of FAS. Our objective was to characterize ADNP in this model to relate this protein to the mechanisms of damage and peptide neuroprotection. Study design: Timed, pregnant C57Bl6/J mice were treated on day 8. Groups were control, alc., peptide pretreatment, or peptide alone. Embryo and decidua were harvested at 6 and 24 h and 10 days. To evaluate ADNP expression, real-time polymerase chain reaction was performed with results presented as the ratio of ADNP-to-glyceraldehyde-3-phosphate dehydrogenase (GAPDH) concentration Anal. of variance was performed for overall comparisons with $P < 0.05$ considered significant. Results: At 6 h, there was no difference in ADNP between alc.-exposed embryos compared with control embryos. At 24 h, there was an increase in ADNP in alc.-exposed embryos compared with controls ($P < .001$); these findings persisted at 10 days ($P < 0.001$). In the decidua at 6 h, there was no difference between alc. and control. At 24 h, there was greater ADNP in alc.-exposed decidua compared with controls ($P < 0.001$), which did not persist at 10 days ($P = 0.97$). Peptide pretreatment did not prevent the alc.-induced increase in ADNP in embryo or decidua. Conclusion: Alc. increased embryonic and decidual ADNP expression at 24 h and it persisted in the embryo for 10 days. Because ADNP is a known neuroprotectant, these findings suggest that it may be released as a protective mechanism in FAS. Changes in the embryo were persistent suggesting that the embryo is more vulnerable to alc.-induced damage than the mother.

IT **177718-96-6 211439-12-2**, NAPVSIPQ
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(activity-dependent neuroprotective protein role in mouse model of **fetal alc. syndrome**)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 03 Oct 2003

ACCESSION NUMBER: 2003:775826 CAPLUS

DOCUMENT NUMBER: 140:36048

TITLE: From vasoactive intestinal peptide (VIP) through activity-dependent neuroprotective protein (ADNP) to NAP. A view of neuroprotection and cell division

AUTHOR(S): Gozes, Illana; Divinsky, Inna; Pilzer, Inbar; Fridkin, Mati; Brenneman, Douglas E.; Spier, Avron D.
CORPORATE SOURCE: Department of Clinical Biochemistry, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv-Jaffa, 69978, Israel
SOURCE: Journal of Molecular Neuroscience (2003), 20(3), 315-322
CODEN: JMNEES; ISSN: 0895-8696
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Accelerated neuronal death brings about cognitive as well as motor and other dysfunctions. A major neuropeptide, vasoactive intestinal peptide (VIP), has been shown to be neuroprotective. However, VIP-based drug design is hampered by the instability of the peptide and its limited bioavailability. Two independent approaches were thus taken to exploit VIP as a lead drug candidate: (1) potent neuroprotective lipophilic analogs of VIP were synthesized, e.g. [stearyl-norleucine-17] VIP (SNV); and (2) potent neuroprotective peptide derivs. were identified that mimic the activity of VIP-responsive neuroprotective glial proteins. VIP provides neuronal defense by inducing the synthesis and secretion of neuroprotective proteins from astrocytes; activity-dependent neuroprotective protein (ADNP) was discovered as such glial cell mediator of VIP- and SNV-induced neuroprotection. In subsequent studies, an eight-amino-acid peptide, NAP, was identified as the smallest active element of ADNP exhibiting potent neuroprotective activities. This paper summarizes the biol. effects of SNV and NAP and further reports advances in NAP studies toward clin. development. An original finding described here shows that NAP, while protecting neurons, demonstrated no apparent effect on cell division in a multiplicity of cell lines, strengthening the notion that NAP is a specific neuroprotective drug candidate.

IT **211439-12-2**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VIP, activity-dependent neuroprotective protein ADNP and NAP in relation to neuroprotection and cell division)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 04 Sep 2003
ACCESSION NUMBER: 2003:688962 CAPLUS
DOCUMENT NUMBER: 139:208245
TITLE: Mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**
INVENTOR(S): Gozes, Illana; Brenneman, Douglas E.; Bassan, Merav; Zamostiano, Rachel
PATENT ASSIGNEE(S): Ramot University Authority for Applied Research and Industrial Development Ltd., Israel; The United States of America, Department of Health and Human Services
SOURCE: U.S., 105 pp., Cont.-in-part of Appl. No. PCT/US98/02485.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6613740	B1	20030902	US 1998-187330	19981106
WO 9835042	A2	19980813	WO 1998-US2485	19980206
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2349159	AA	20000518	CA 1999-2349159	19991104
WO 2000027875	A2	20000518	WO 1999-US26213	19991104
WO 2000027875	A3	20000727		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1124960	A2	20010822	EP 1999-971817	19991104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 776833	B2	20040923	AU 2000-14698	19991104
US 2004053313	A1	20040318	US 2003-623272	20030717

PRIORITY APPLN. INFO.:	US 1997-37404P	P	19970207
	WO 1998-US2485	A2	19980206
	US 1998-187330	A	19981106
	WO 1999-US26213	W	19991104

OTHER SOURCE(S): MARPAT 139:208245

AB The present invention relates generally to Activity Dependent Neurotrophic Factor III (ADNF III), also known as Activity Dependent Neuroprotective Protein (ADNP). More particularly, the present invention relates to nucleic acid sequences encoding ADNF III polypeptides; ADNF III polypeptides encoded by such nucleic acid sequences; antibodies to ADNF III polypeptides; and methods of using such ADNF III polypeptides for the treatment of neurol. deficiencies and for the prevention of cell death associated with (1) gp120, the envelope protein from HIV; (2) N-methyl-D-aspartic acid (excito-toxicity); (3) tetrodotoxin (blockage of elec. activity); and (4) β-amyloid peptide, a substance related to neuronal degeneration in Alzheimer's disease. The mouse and human ADNF III cDNAs were cloned and sequenced. An ADNF III-derived octapeptide, NAPVSIPQ, mimicked the activity of the total protein in a neurodegeneration model system (ApoE-deficient homozygous mice) and a rat model of cholinergic deficiency. Claimed sequences are inadequately identified in the document.

IT **590465-44-4D**, N- and C-terminal extension derivs.
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence, activity-dependent neurotrophic factor III; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

IT **590465-45-5 590465-46-6 590465-47-7 590465-48-8 590465-49-9**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

IT **177159-38-5 177718-96-6 211439-10-0 211439-12-2 270084-37-2 270084-38-3 292039-06-6 292039-07-7 292039-08-8 590516-42-0 590516-43-1 590516-45-3**
RL: PRP (Properties)
(unclaimed protein sequence; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 21 Jul 2003
ACCESSION NUMBER: 2003:555487 CAPLUS
DOCUMENT NUMBER: 139:209175
TITLE: Differential effects of ethanol antagonism and neuroprotection in peptide fragment NAPVSIPQ prevention of ethanol-induced developmental toxicity
AUTHOR(S): Wilkemeyer, Michael F.; Chen, Shao-yu; Menkari, Carrie E.; Brenneman, Douglas E.; Sulik, Kathleen K.; Charness, Michael E.
CORPORATE SOURCE: Veterans Affairs Boston Healthcare System, Neurology Service, West Roxbury, MA, 02132, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(14), 8543-8548
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB NAPVSIPQ (NAP), an active fragment of the glial-derived activity-dependent neuroprotective protein, is protective at femtomolar concns. against a wide array of neural insults and prevents ethanol-induced fetal wastage and growth retardation in mice. NAP also antagonizes ethanol inhibition of L1-mediated cell adhesion (ethanol antagonism). We performed an Ala scanning substitution of NAP to determine the role of ethanol antagonism and neuroprotection in NAP prevention of ethanol embryotoxicity. The Ser-Ile-Pro region of NAP was crucial for both ethanol antagonism and protection of cortical neurons from tetrodotoxin toxicity (neuroprotection). Ala replacement of either Ser-5 or Pro-7 (P7A-NAP) abolished NAP neuroprotection but minimally changed the efficacy of NAP ethanol antagonism. In contrast, Ala replacement of Ile-6 (I6A-NAP) caused a decrease in potency (>2 logarithmic orders) with only a small reduction (<10%) in the efficacy of NAP neuroprotection but markedly reduced the efficacy (50%) and the potency (5 logarithmic orders) of NAP ethanol antagonism. Ethanol significantly reduced the number of paired somites in

mouse whole-embryo culture; this effect was prevented significantly by 100 pM NAP or by 100 pM P7A-NAP, but not by 100 pM I6A-NAP. The structure-activity relation for NAP prevention of ethanol embryotoxicity was similar to that for NAP ethanol antagonism and different from that for NAP neuroprotection. These findings support the hypothesis that NAP antagonism of ethanol inhibition of L1 adhesion plays a central role in NAP prevention of ethanol embryotoxicity and highlight the potential importance of ethanol effects on L1 in the pathophysiol. of **fetal alc. syndrome.**

IT **211439-12-2**, NAPVSIPQ
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(differential effects of ethanol antagonism and neuroprotection in peptide fragment NAPVSIPQ prevention of ethanol-induced developmental toxicity in human L1-transfected NIH/3T3 cells)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 03 Oct 2002
ACCESSION NUMBER: 2002:749911 CAPLUS
DOCUMENT NUMBER: 138:282681
TITLE: Peptide antagonists of ethanol inhibition of L1-mediated cell-cell adhesion
AUTHOR(S): Wilkemeyer, Michael F.; Menkari, Carrie E.; Spong, Catherine Y.; Charness, Michael E.
CORPORATE SOURCE: Department of Neurology, Brigham and Women's Hospital, Boston, MA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 303(1), 110-116
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ethanol inhibits cell-cell adhesion mediated by the L1 cell adhesion mol. 1-Octanol potently antagonizes this cellular action of ethanol and also prevents ethanol-induced dysmorphol. and cell death in mouse whole embryo culture. NAPVSIPQ (NAP) and SALLRSIPA (SAL) are active peptide fragments of two neuroprotective proteins: activity-dependent neuroprotective protein and activity-dependent neurotrophic factor. NAP and SAL are neuroprotective at femtomolar concns. against a variety of neurotoxins and also prevent ethanol teratogenesis in mice. To explore the cellular basis for this action, we asked whether NAP and SAL antagonize ethanol inhibition of L1 adhesion. Aggregation assays were carried out in ethanol-sensitive, human L1-transfected NIH/3T3 cells in the absence and presence of NAP and SAL. Neither NAP nor SAL altered L1 adhesion or L1 expression; however, both peptides potently and completely antagonized the inhibition of L1 adhesion by 100 mM ethanol (EC50: NAP, 6+10-14 M; SAL, 4+10-11 M). NAP also antagonized ethanol inhibition of cell-cell adhesion in bone morphogenetic protein-7-treated NG108-15 cells. In L1-expressing NIH/3T3 cells, SAL antagonism was reversible and could be overcome by increasing concns. of ethanol. In contrast, NAP antagonism was irreversible and could not be overcome by increasing agonist concentration
Two scrambled NAP peptides (ASPNQPIV and PNIQVASP) were not antagonists at

concns. as high as 10-7 M. Thus, two structurally unrelated classes of compds., alcs. and small polypeptides, share two common actions: antagonism of ethanol inhibition of L1-mediated cell adhesion and prevention of ethanol teratogenesis. These findings support the hypothesis that ethanol inhibition of L1 adhesion contributes to ethanol teratogenesis.

IT **211439-12-2**, NAPVSIPQ
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NAP peptide; peptide antagonists of ethanol inhibition of L1-mediated cell-cell adhesion)

IT **177718-96-6**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SAL peptide; peptide antagonists of ethanol inhibition of L1-mediated cell-cell adhesion)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 28 Aug 2001
ACCESSION NUMBER: 2001:623335 CAPLUS
DOCUMENT NUMBER: 135:299083
TITLE: Neurotrophins prevent HIV Tat-induced **neuronal apoptosis** via a nuclear factor-κB (NF-κB)-dependent mechanism
AUTHOR(S): Ramirez, Servio H.; Sanchez, Joseph F.; Dimitri, Christopher A.; Gelbard, Harris A.; Dewhurst, Stephen; Maggirwar, Sanjay B.
CORPORATE SOURCE: Departments of Microbiology and Immunology, University of Rochester Medical Center, Rochester, NY, 14642, USA
SOURCE: Journal of Neurochemistry (2001), 78(4), 874-889
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB HIV-1 associated dementia is thought to be caused by neuronal damage and death in response to the production of soluble neurotoxic factors by virally infected mononuclear phagocytes. These neurotoxins include HIV-1 Tat. The ability of neurotrophins to promote cell survival prompted the authors to examine whether neurotrophins might also be capable of opposing the pro-apoptotic effects of Tat. Here, the authors show that Tat-induced **neuronal apoptosis** in primary cultures of rat cerebellar granule cells and in neuronally differentiated human SK-N-MC cells is profoundly inhibited by brain-derived neurotrophic factor, nerve growth factor and activity-dependent neurotrophic factor nonamer peptide. These neurotrophins activated the transcription factor NF-κB, and inhibition of NF-κB activation using a super-repressor IκB-α mutant was found to block the survival-promoting activity of the neurotrophins. Reporter gene assays and immunoblot expts. revealed that the neurotrophins also up-regulated the expression of Bcl-2, at both the transcriptional and protein levels. Overexpression of the super-repressor IκB-α mutant prevented this induction of Bcl-2 expression. Moreover, overexpression of either Bcl-2, alone, or the RelA subunit of NF-κB, alone, protected **neurons** from Tat-induced **apoptosis**. These findings suggest that the

activation of NF-κB by neurotrophic factors may promote survival of neurons exposed to Tat, via regulation of anti-apoptotic genes including Bcl-2.

IT **177718-96-6**, Activity-dependent neurotrophic factor peptide 9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(neurotrophins prevent HIV Tat-induced **neuronal apoptosis** via a nuclear factor-κB-dependent mechanism)

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 07 May 2001
ACCESSION NUMBER: 2001:321648 CAPLUS
DOCUMENT NUMBER: 134:362624
TITLE: Prevention of fetal demise and growth restriction in a mouse model of **fetal alcohol syndrome**
AUTHOR(S): Spong, Catherine Y.; Abebe, Daniel T.; Gozes, Illana; Brenneman, Douglas E.; Hill, Joanna M.
CORPORATE SOURCE: Section on Developmental and Molecular Pharmacology, Laboratory of Developmental Neurobiology, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2001), 297(2), 774-779
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two peptides [NAPVSIPQ (NAP) and SALLRSIPA (ADNF-9)], that are associated with novel glial proteins regulated by vasoactive intestinal peptide, are shown now to provide protective intervention in a model of **fetal alc. syndrome**. Fetal demise and growth restrictions were produced after the i.p. injection of ethanol to pregnant mice during mid-gestation (E8). Death and growth abnormalities elicited by alc. treatment during development are believed to be associated, in part, with severe oxidative damage. NAP and ADNF-9 have been shown to exhibit antioxidative and antiapoptotic actions in vitro. Pretreatment with an equimolar combination of the peptides prevented the alc.-induced fetal death and growth abnormalities. Pretreatment with NAP alone resulted in a significant decrease in alc.-associated fetal death; whereas ADNF-9 alone had no detectable effect on fetal survival after alc. exposure, indicating a pharmacol. distinction between the peptides. Biochem. assessment of the fetuses indicated that the combination peptide treatment prevented the alc.-induced decreases in reduced glutathione. Peptide efficacy was evident with either 30-min pretreatment or with 1-h post-alc. administration. Bioavailability studies with [3H]NAPVSIPQ indicated that 39% of the total radioactivity comigrated with intact peptide in the fetus 60 min after administration. These studies demonstrate that fetal death and growth restriction associated with prenatal alc. exposure were prevented by combinatorial peptide treatment and suggest that this therapeutic strategy be explored in other models/diseases associated with oxidative stress.

IT **211439-12-2**, NAPVSIPQ
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prevention of fetal demise and growth restriction in mouse model of **fetal alc. syndrome**)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 25 Feb 2001
ACCESSION NUMBER: 2001:137237 CAPLUS
DOCUMENT NUMBER: 134:198025
TITLE: Orally active peptides that prevent cell damage and death
INVENTOR(S): Brenneman, Douglas E.; Gozes, Illana; Spong, Catherine Y.; Pinhasov, Albert; Giladi, Eliezer
PATENT ASSIGNEE(S): Ramot University Authority for Applied Research & Industrial Development, Israel; United States Dept. of Health and Human Services
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012654	A2	20010222	WO 2000-US22861	20000817
WO 2001012654	A3	20020124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2381981	AA	20010222	CA 2000-2381981	20000817
AU 2000069201	A5	20010313	AU 2000-69201	20000817
AU 761597	B2	20030605		
EP 1206489	A2	20020522	EP 2000-957607	20000817
EP 1206489	B1	20040506		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
AT 266044	E	20040515	AT 2000-957607	20000817
ES 2220522	T3	20041216	ES 2000-957607	20000817
PRIORITY APPLN. INFO.:			US 1999-149956P P	19990818
			WO 2000-US22861 W	20000817

AB This invention provides an ADNF (activity-dependent neurotrophic factor) polypeptide comprising an active core site, the active core site comprising at least one D-amino acid. The invention also provides a pharmaceutical composition comprising an ADNF polypeptide comprising an active
core site, the active core site comprising at least one D-amino acid. In

particular, the pharmaceutical composition of the invention is orally active.

The invention further provides methods for reducing **neuronal cell death**, methods for reducing oxidative stress, and methods for reducing a condition associated with **fetal alc . syndrome** using the ADNF polypeptides and the pharmaceutical compns. of the invention.

IT **177159-38-5 177718-96-6 209051-20-7 209051-27-4 211439-10-0 211439-12-2 292039-03-3 292039-04-4 292039-05-5 292039-06-6 292039-07-7 292039-08-8 327157-61-9 327157-62-0 327157-63-1**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(orally active peptides that prevent cell damage and death)

L3 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 19 Jan 2001

ACCESSION NUMBER: 2001:45165 CAPLUS

DOCUMENT NUMBER: 134:120910

TITLE: Neurotrophic peptides of activity-dependent neurotrophic factor

INVENTOR(S): Brenneman, Douglas E.

PATENT ASSIGNEE(S): Ramot University Authority for Applied Research and Industrial Development, Israel; The United States of America as Represented by the Department of Health and Human Services

SOURCE: U.S., 32 pp., Cont.-in-part of U.S. 5,767,240.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6174862	B1	20010116	US 1994-324297	19941017
US 688087	A0	19920101	US 1991-688087	19910422
US 5767240	A	19980616	US 1992-871973	19920422
CA 2202496	AA	19960425	CA 1995-2202496	19951016
WO 9611948	A1	19960425	WO 1995-US12929	19951016
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9537641	A1	19960506	AU 1995-37641	19951016
AU 707838	B2	19990722		
EP 797590	A1	19971001	EP 1995-935735	19951016
EP 797590	B1	20020123		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 10509428	T2	19980914	JP 1995-513344	19951016
AT 212359	E	20020215	AT 1995-935735	19951016

PRIORITY APPLN. INFO.: US 1991-688087 B2 19910422
US 1992-871973 A2 19920422
US 1994-324297 A 19941017
WO 1995-US12929 W 19951016

OTHER SOURCE(S): MARPAT 134:120910

AB The present invention relates generally to Activity-Dependent Neurotrophic Factor (ADNF). More particularly, the present invention relates to a family of polypeptides derived from ADNF that exhibit neuroprotective/neurotrophic action on neurons originating in the central nervous system and to uses thereof for the treatment of neurol. deficiencies and for the prevention of cell death. The present invention also relates to pharmaceutical compns. designed to prevent **neuronal cell death.**

IT **177159-38-5 177718-96-6 209051-20-7 209051-27-4 320609-76-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(neurotrophic peptides of activity-dependent neurotrophic factor)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 15 Sep 2000
ACCESSION NUMBER: 2000:645879 CAPLUS
DOCUMENT NUMBER: 133:233267
TITLE: Prevention of **fetal alcohol syndrome** and **neuronal cell death** with ADNF polypeptides
INVENTOR(S): Brenneman, Douglas E.; Spong, Catherine Y.; Gozes, Illana; Bassan, Merav; Zamostiano, Rachel
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; Ramot of Tel Aviv University
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000053217	A2	20000914	WO 2000-US6364	20000310
WO 2000053217	A3	20010111		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002111301	A1	20020815	US 1999-267511	19990312

PRIORITY APPLN. INFO.: US 1999-267511 A 19990312

AB The invention relates to methods for reducing a condition associated with **fetal alc. syndrome** in a subject who is exposed to alc. in utero with an ADNF (activity dependent neurotrophic factors) polypeptide (e.g, ADNF I polypeptides, ADNF III polypeptides, or mixts. of ADNF I and ADNF III polypeptides). The ADNF polypeptide of the invention is selected from the group consisting of: (a) an ADNF I polypeptide comprising an active core site having the following amino acid sequence: Ser-Ala-Leu-Leu-Arg-Ser-Ile-Pro-Ala (SEQ ID NO: 1); (b) an ADNF III polypeptide comprising an active core site having the following amino acid sequence: Asn-Ala-Pro-Val-Ser-Ile-Pro-Gln (SEQ ID NO:2); and (c) a mixture of the ADNF I polypeptide of part (a) and the ADNF III polypeptide of part (b). The **fetal alc. syndrome** condition that is treated is decreased body weight, decreased brain weight, decreased level of VIP mRNA or protein, decreased viability, or decreased learning. The present invention further relates to methods for reducing **neuronal cell death** by contacting **neuronal** cells with a mixture of ADNF I and ADNF III polypeptides. At least one of the ADNF polypeptides can be encoded by a nucleic acid which is administered to the subject. Still further, the present invention relates to a pharmaceutical composition comprising a mixture of ADNF I and ADNF III polypeptides.

IT **177159-38-5P 177718-96-6P 209051-20-7P 209051-27-4P 211439-10-0P 211439-12-2P 292039-03-3P 292039-04-4P 292039-05-5P 292039-06-6P 292039-07-7P 292039-08-8P**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prevention of conditions associated with **fetal alc. syndrome** and **neuronal cell death** with ADNF polypeptides)

L3 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 28 Jun 2000
ACCESSION NUMBER: 2000:429944 CAPLUS
DOCUMENT NUMBER: 133:130186
TITLE: Nuclear factor-κB mediates the cell survival-promoting action of activity-dependent neurotrophic factor peptide-9
AUTHOR(S): Glazner, Gordon W.; Camandola, Simonetta; Mattson, Mark P.
CORPORATE SOURCE: Sanders-Brown Research Center on Aging and Department of Anatomy and Neurobiology, University of Kentucky, Lexington, KY, USA
SOURCE: Journal of Neurochemistry (2000), 75(1), 101-108
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activity-dependent neurotrophic factor (ADNF) is produced by astrocytes in response to neuronal depolarization and, in turn, promotes neuronal survival. A nine-amino acid ADNF peptide (ADNF9) exhibits full neurotrophic activity and potently protects cultured embryonic rat hippocampal **neurons** from oxidative injury and **apoptosis**

. Picomolar concns. of ADNF9 induced an increase in nuclear factor-κB (NF-κB) DNA-binding activity within 1 h of exposure, with a maximum increase of .apprx.10-fold by 6 h. Activation of NF-κB was correlated with increased resistance of **neurons** to **apoptosis** induced by exposure to Fe2+. The antiapoptotic action of ADNF9 was abolished when NF-κB activation was specifically blocked with κB decoy DNA. Oxidative stress was attenuated in neurons pretreated with ADNF9, and this effect of ADNF9 was blocked by κB decoy DNA, suggesting that ADNF9 suppresses apoptosis by reducing oxidative stress. ADNF9 also prevented **neuronal apoptosis** following trophic factor withdrawal via an NF-κB-mediated mechanism. Thus, NF-κB mediates the neuron survival-promoting effects of ADNF9 in exptl. models relevant to developmental neuronal death and neurodegenerative disorders.

IT **177718-96-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(nuclear factor-κB mediates cell survival-promoting action of activity-dependent neurotrophic factor peptide-9 in rat hippocampal neurons)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 06 Jun 2000
ACCESSION NUMBER: 2000:373753 CAPLUS
DOCUMENT NUMBER: 133:84725
TITLE: Activity-dependent neurotrophic factor: intranasal administration of femtomolar-acting peptides improve performance in a water maze
AUTHOR(S): Gozes, Illana; Giladi, Eliezer; Pinhasov, Albert; Bardea, Amos; Brenneman, Douglas E.
CORPORATE SOURCE: Department of Clinical Biochemistry, Sackler School of Medicine, Tel Aviv University, Tel Aviv-Jaffa, Israel
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 293(3), 1091-1098
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activity-dependent neurotrophic factor (ADNF) is a glia-derived protein that is neuroprotective at femtomolar concns. A nine-amino acid peptide derived from ADNF (Ser-Ala-Leu-Leu-Arg-Ser-Ile-Pro-Ala; ADNF-9) captured the activity of the parent protein and has been reported to protect cultured neurons from multiple neurotoxins. Antibodies recognizing ADNF-9 produced **neuronal apoptosis**, and identified an addnl., structurally related, glia-derived peptide, Asn-Ala-Pro-Val-Ser-Ile-Pro-Gln (NAP). Previous comparative studies have characterized s.c.-injected NAP as most efficacious in protecting against developmental retardation and learning impairments in apolipoprotein E-deficient mice. This study was designed to assess (1) neuroprotection after intranasal administration of ADNF-9 and NAP to rats treated with the cholinotoxin ethylcholine aziridium; and (2) bioavailability and pharmacokinetics after intranasal administration. Results showed significant improvements in short-term spatial memory, as assessed in a water maze, after daily intranasal

administration of 1 μg of peptide (ADNF-9 or NAP) per animal. However, a 5-day pretreatment with ADNF-9 did not improve performance measured after cessation of treatment. Compared with rats treated with ADNF-9, NAP-pre-treated animals exhibited a significantly better performance. Furthermore, NAP (and not ADNF-9) protected against loss of choline acetyltransferase activity. Significant amts. of 3H-labeled NAP reached the brain, remained intact 30 min after administration, and dissipated 60 min after administration. This study revealed efficacy for ADNF-related peptides in rodent models for neurodegeneration. The small size of the mols., the low dosage required, the noninvasive administration route, and the demonstrated activity in a relevant paradigm suggest NAP as a lead compound for future drug design.

IT **177718-96-6 211439-12-2**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(activity-dependent neurotrophic factor derivative intranasal administration pharmacokinetics, metabolism and neuroprotection and effect on memory and learning)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 19 May 2000
ACCESSION NUMBER: 2000:335438 CAPLUS
DOCUMENT NUMBER: 133:1200
TITLE: Mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**
INVENTOR(S): Gozes, Illana; Brenneman, Douglas E.; Bassan, Merav; Zamostiano, Rachel
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; Ramot University Authority for Applied Research and Industrial Development
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027875	A2	20000518	WO 1999-US26213	19991104
WO 2000027875	A3	20000727		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6613740	B1	20030902	US 1998-187330	19981106

CA 2349159	AA	20000518	CA 1999-2349159		19991104
EP 1124960	A2	20010822	EP 1999-971817		19991104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
AU 776833	B2	20040923	AU 2000-14698		19991104
PRIORITY APPLN. INFO.:			US 1998-187330	A	19981106
			US 1997-37404P	P	19970207
			WO 1998-US2485	A2	19980206
			WO 1999-US26213	W	19991104

OTHER SOURCE(S): MARPAT 133:1200

AB The present invention relates generally to Activity Dependent Neurotrophic Factor III (ADNF III), also known as Activity Dependent Neuroprotective Protein (ADNP). More particularly, the present invention relates to nucleic acid sequences encoding ADNF III polypeptides; ADNF III polypeptides encoded by such nucleic acid sequences; antibodies to ADNF III polypeptides; and methods of using such ADNF III polypeptides for the treatment of neurol. deficiencies and for the prevention of cell death associated with (1) gp120, the envelope protein from HIV; (2) N-methyl-D-aspartic acid (excito-toxicity); (3) tetrodotoxin (blockage of elec. activity); and (4) β-amyloid peptide, a substance related to neuronal degeneration in Alzheimer's disease. The rat and human ADNF III cDNAs were cloned and sequenced. An ADNF III-derived octapeptide, NAPVSIPQ, mimicked the activity of the total protein in a neurodegeneration model system (ApoE-deficient homozygous mice) and a rat model of cholinergic deficiency. Claimed sequences are inadequately identified in the document.

IT **211439-12-2D**, conjugates
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(ADNF III peptide; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

IT **211681-43-5 211681-48-0**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

IT **177159-38-5 177718-96-6 211439-12-2 223533-74-2 270084-37-2 270084-38-3 270898-03-8 270898-05-0**
RL: PRP (Properties)
(unclaimed sequence; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

L3 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 01 Mar 2000
ACCESSION NUMBER: 2000:138163 CAPLUS
DOCUMENT NUMBER: 132:217349
TITLE: Vasoactive intestinal peptide (VIP) prevents neurotoxicity in neuronal cultures: relevance to neuroprotection in Parkinson's disease
AUTHOR(S): Offen, Daniel; Sherki, Yossi; Melamed, Eldad; Fridkin,

Mati; Brenneman, Douglas E.; Gozes, Illana
CORPORATE SOURCE: Department of Clinical Biochemistry and Felsentein Medical Research Center, Rabin Medical Center, The Sackler Faculty of Medicine, Department of Neurology and Felsentein Medical Research Center, Tel Aviv University, Tel Aviv-Jaffa, 69978, Israel
SOURCE: Brain Research (2000), 854(1,2), 257-262
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Vasoactive intestinal peptide (VIP) provides neuroprotection against β-amyloid toxicity in models of Alzheimer's disease. A superactive analog, stearylNle 17-VIP (SNV) is a 100-fold more potent than VIP. In primary neuronal cultures, VIP protective activity may be mediated by femtomolar-acting glial proteins such as activity-dependent neurotrophic factor (ADNF), activity-dependent neuroprotective protein (ADNP), peptide derivs. ADNF-9 (9aa) and NAP (8aa), resp. It has been hypothesized that β-amyloid induces oxidative stress leading to **neuronal cell death**. Similarly, dopamine and its oxidation products were suggested to trigger dopaminergic nigral cell death in Parkinson's disease. The authors now examined the possible protective effects of VIP against toxicity of dopamine, 6-hydroxydopamine (6-OHDA) and 1-methyl-4-phenylpyridinium ion (MPP+) in neuronal cultures [rat pheochromocytoma (PC12), human neuroblastoma (SH-SY5Y) and rat cerebellar granular cells]. Remarkably low concns. of VIP (10-16-10-8 M), ADNF-9 and NAP (10-18-10-10 M) protected against dopamine and 6-OHDA toxicity in PC12 and neuroblastoma cells. VIP (10-11-10-9 M) and SNV (10-13-10-11 M), protected cerebellar granule neurons against 6-OHDA. In contrast, VIP did not rescue neurons from death associated with MPP+. Since dopamine toxicity is linked to the red/ox state of the cellular glutathione, the authors investigated neuroprotection in cells depleted of reduced glutathione (GSH). Buthionine sulfoximine (BSO), a selective inhibitor of glutathione synthesis, caused a marked reduction in GSH in neuroblastoma cells and their viability decreased by 70-90%. VIP, SNV or NAP (over a wide concentration range) provided significant neuroprotection against BSO toxicity. These results show that the mechanism of neuroprotection by VIP/SNV/NAP may be mediated through raising cellular resistance against oxidative stress. The authors' data suggest these compds. as potential lead compds. for protective therapies against Parkinson's disease.

IT **177718-96-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(VIP prevention of neurotoxicity in neuronal cultures and involved mechanisms in relation to neuroprotection in Parkinson's disease)

IT **211439-12-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VIP prevention of neurotoxicity in neuronal cultures and involved mechanisms in relation to neuroprotection in Parkinson's disease)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 24 CAPLUS

ED Entered STN: 24 Feb 2000
ACCESSION NUMBER: 2000:127460 CAPLUS
DOCUMENT NUMBER: 132:330286
TITLE: Differential Effects of BDNF, ADNF9, and TNFα on Levels of NMDA Receptor Subunits, Calcium Homeostasis, and Neuronal Vulnerability to Excitotoxicity
AUTHOR(S): Glazner, Gordon W.; Mattson, Mark P.
CORPORATE SOURCE: Sanders-Brown Research Center on Aging and Department of Anatomy and Neurobiology, University of Kentucky, Lexington, KY, 40536, USA
SOURCE: Experimental Neurology (2000), 161(2), 442-452
CODEN: EXNEAC; ISSN: 0014-4886
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Calcium influx through N-methyl-D-aspartate (NMDA) receptors can result in **neuronal apoptosis** or necrosis and may play a pivotal role in neuronal death in many different neurodegenerative diseases. In the present study the authors employed primary neuronal cultures and three different excitoprotective factors, brain-derived neurotrophic factor (BDNF), activity-dependent neurotrophic factor (ADNF9), and tumor necrosis factor α (TNFα), to elucidate the mechanisms whereby trophic factors modify the excitotoxic process. Neurons pretreated with BDNF exhibited increased levels of the NMDA receptor subunits NR1 and NR2A, which was associated with increased calcium responses to NMDA and vulnerability to excitotoxic necrosis and reduced vulnerability to apoptosis. ADNF9 and TNFα suppressed calcium responses to glutamate and protected **neurons** against both excitotoxic necrosis and **apoptosis**, but had no effect on levels of NMDA receptor subunits. Inhibition of phosphorylation and DNA binding of NF-κB, by H7 and κB decoy DNA, resp., suggest that the excitotoxic-modulating actions of BDNF are mediated by kinases, while those of ADNF9 and TNFα are mediated by both kinases and the transcription factor NF-κB. The authors' data show that, whereas BDNF increases neuronal responses to glutamate while ADNF9 and TNFα decrease the same, all three protect against excitotoxic apoptosis. (c) 2000 Academic Press.

IT **177718-96-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(BDNF and ADNF9 and TNFα differential effects on levels of NMDA receptor subunits and calcium homeostasis and neuronal vulnerability to excitotoxicity)

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 03 Dec 1999
ACCESSION NUMBER: 1999:763280 CAPLUS
DOCUMENT NUMBER: 132:59555
TITLE: Activity-dependent neurotrophic factor peptide (ADNF9) protects neurons against oxidative stress-induced death
AUTHOR(S): Glazner, Gordon W.; Boland, Andre; Dresse, Albert E.; Brenneman, Douglas E.; Gozes, Illana; Mattson, Mark P.
CORPORATE SOURCE: Sanders-Brown Research Center on Aging and Department of Anatomy and Neurobiology, University of Kentucky,

Lexington, KY, 40536-0230, USA
SOURCE: Journal of Neurochemistry (1999), 73(6), 2341-2347
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Activity-dependent neurotrophic factor (ADNF) and a 14-amino acid fragment of this peptide (sequence VLGGGSALLRSIPA) protect neurons from death associated with an array of toxic conditions, including amyloid β-peptide, N-methyl-D-aspartate, tetrodotoxin, and the neurotoxic HIV envelope coat protein gp 120. The authors report that an even smaller, nine-amino acid fragment (ADNF9) with the sequence SALLRSIPA potently protects cultured embryonic day 18 rat hippocampal **neurons** from oxidative injury and **neuronal apoptosis** induced by FeSO4 and trophic factor withdrawal. Among the characteristics of this protection are maintenance of mitochondrial function and a reduction in accumulation of intracellular reactive oxygen species.
IT **177718-96-6**, Activity-dependent neurotrophic factor peptide-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(activity-dependent neurotrophic factor peptide ADNF9 protects neurons against oxidative stress-induced death)
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 26 Apr 1999
ACCESSION NUMBER: 1999:254850 CAPLUS
DOCUMENT NUMBER: 131:54308
TITLE: A femtomolar-acting neuroprotective peptide induces increased levels of heat shock protein 60 in rat cortical neurons: a potential neuroprotective mechanism
AUTHOR(S): Zamostiano, Rachel; Pinhasov, Albert; Bassan, Merav; Perl, Orly; Steingart, Ruth A.; Atlas, Roy; Brenneman, Douglas E.; Gozes, Illana
CORPORATE SOURCE: Sackler School of Medicine, Department of Clinical Biochemistry, Tel Aviv University, Tel Aviv-Jaffa, 69978, Israel
SOURCE: Neuroscience Letters (1999), 264(1,2,3), 9-12
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Activity-dependent neurotrophic factor (ADNF) was recently isolated from conditioned media of astrocytes stimulated with VIP. ADNF provided neuroprotection at femtomolar concentration against a wide variety of toxic insults. A nine amino acid peptide (ADNF-9) captured with even greater potency the neuroprotective activity exhibited by the parent protein. Utilizing Northern and Western blot analyses, it was now shown that ADNF-9 increased the expression of heat shock protein 60 (hsp60) in rat cerebral cortical cultures. In contrast, treatment with the Alzheimer's toxin, the β-amyloid peptide, reduced the amount of intracellular hsp60. Treatment with ADNF-9 prevented the reduction in hsp60 produced by the β-amyloid peptide. The protection against the β-amyloid peptide-associated cell death provided by ADNF-9 may be mediated in part by

intracellular increases in hsp60.

IT **177718-96-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(activity-dependent neurotrophic factor nanopeptide neuroprotection mediation by increases in HSP60)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 31 Aug 1998
ACCESSION NUMBER: 1998:550513 CAPLUS
DOCUMENT NUMBER: 129:185098
TITLE: Mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**
INVENTOR(S): Gozes, Illana; Brenneman, Douglas E.; Bassan, Merav
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9835042	A2	19980813	WO 1998-US2485		19980206
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2279231	AA	19980813	CA 1998-2279231		19980206
AU 9863222	A1	19980826	AU 1998-63222		19980206
AU 737406	B2	20010816			
EP 966533	A1	19991229	EP 1998-907407		19980206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2001522228	T2	20011113	JP 1998-534982		19980206
US 6613740	B1	20030902	US 1998-187330		19981106
US 2004053313	A1	20040318	US 2003-623272		20030717
PRIORITY APPLN. INFO.:			US 1997-37404P	P	19970207
			WO 1998-US2485	W	19980206
			US 1998-187330	A3	19981106

AB The present invention relates generally to Activity Dependent Neurotrophic Factor III (ADNF III), also known as Activity Dependent Neuroprotective Protein (ADNP). More particularly, the present invention relates to nucleic acid sequences encoding ADNF III polypeptides; ADNF III polypeptides encoded by such nucleic acid sequences; antibodies to ADNF III polypeptides; and methods of using such ADNF III polypeptides for the treatment of neurol. deficiencies and for the prevention of cell death

associated with (1) gp120, the envelope protein from HIV; (2) N-methyl-D-aspartic acid (excito-toxicity); (3) tetrodotoxin (blockage of elec. activity); and (4) β-amyloid peptide, a substance related to neuronal degeneration in Alzheimer's disease. The rat and human ADNF III cDNAs were cloned and sequenced. ADNF III protected against tetrodotoxin and β-amyloid peptide toxicity at femtomolar concns. in cerebral cortical cultures. An ADNF III-derived octapeptide, NAPVSIPQ, mimiced the activity of the total protein in a neurodegeneration model system (ApoE-deficient homozygous mice) and a rat model of cholinergic deficiency.

IT **211439-10-0 211439-12-2**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(ADNF III peptide; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

IT **211681-43-5 211681-48-0**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; mammalian activity-dependent neurotrophic factor III and its cDNA and methods for prevention of **neuronal cell death**)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 15 Mar 1997
ACCESSION NUMBER: 1997:177635 CAPLUS
DOCUMENT NUMBER: 126:259561
TITLE: Antiserum to activity-dependent neurotrophic factor produces **neuronal cell death** in CNS cultures: immunological and biological specificity
AUTHOR(S): Gozes, Illana; Davidson, Ariane; Gozes, Yehoshua; Mascolo, Richard; Barth, Rolf; Warren, Dale; Hauser, Janet; Brenneman, Douglas E.
CORPORATE SOURCE: Department of Clinical Biochemistry, Sackler School of Medicine, Tel Aviv University, Tel Aviv-Jaffa, Israel
SOURCE: Developmental Brain Research (1997), 99(2), 167-175
CODEN: DBRRDB; ISSN: 0165-3806
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activity-dependent neurotrophic factor (ADNF) is a glia-derived protein that is neuroprotective at femtomolar concns. ADNF is released from astroglia after treatment with 0.1 nM vasoactive intestinal peptide (VIP). To further assess the biol. role of ADNF, antiserum was produced following sequential injections of purified ADNF into mice. Anti-ADNF ascites fluid (1:10,000) decreased neuronal survival by 45-55% in comparison to untreated cultures or those treated with control ascites. The neuronal death after anti-ADNF treatment was observed in cultures derived from the spinal cord, hippocampus or cerebral cortex at similar IC50's. Using a terminal deoxynucleotidyl transferase in situ assay to estimate apoptosis in cerebral cortical cultures, anti-ADNF was shown to produce a 70% increase

in the number of labeled cells in comparison to controls. In spinal cord cultures, anti-ADNF treatment produced a 20% decrease in choline acetyltransferase activity in comparison to controls. **Neuronal cell death** produced by the antiserum to ADNF was prevented in cultures co-treated with purified ADNF or ADNF-15, an active peptide derived from the parent ADNF. In vitro binding between the anti-ADNF and ADNF-15 was demonstrated with size exclusion chromatog. Comparative studies with other growth factors (insulin-like growth factor-1, platelet-derived growth factor, nerve growth factor, epidermal growth factor, ciliary neurotrophic growth factor, and neurotrophin-3) demonstrated that only ADNF prevented **neuronal cell death** associated with elec. blockade. These investigations indicated that an ADNF-like substance was present in cultures derived from multiple locations in the central nervous system and that ADNF-15 exhibited both neuroprotection and immunogenicity. ADNF appears to be both a regulator of activity-dependent neuronal survival and a neuroprotectant.

IT **188781-55-7**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activity-dependent neurotrophic factor antiserum produces **neuronal cell death** in CNS cultures)

L3 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 22 Jun 1996
ACCESSION NUMBER: 1996:363612 CAPLUS
DOCUMENT NUMBER: 125:26945
TITLE: Neurotrophic peptides of activity dependent neurotrophic factor
INVENTOR(S): Brenneman, Douglas E.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9611948	A1	19960425	WO 1995-US12929	19951016
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6174862	B1	20010116	US 1994-324297	19941017
CA 2202496	AA	19960425	CA 1995-2202496	19951016
AU 9537641	A1	19960506	AU 1995-37641	19951016
AU 707838	B2	19990722		
EP 797590	A1	19971001	EP 1995-935735	19951016
EP 797590	B1	20020123		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 10509428	T2	19980914	JP 1995-513344	19951016

AT 212359	E	20020215	AT 1995-935735		19951016
PRIORITY APPLN. INFO.:			US 1994-324297	A	19941017
			US 1991-688087	B2	19910422
			US 1992-871973	A2	19920422
			WO 1995-US12929	W	19951016

AB The present invention relates generally to activity dependent neurotrophic factor (ADNF). More particularly, the present invention relates to a family of polypeptides derived from ADNF that exhibit neuroprotective/neuroprotective/neurotrophic action on neurons originating in the central nervous system and to uses thereof for the treatment of neurol. deficiencies and for the prevention of cell death. The present invention also relates to pharmaceutical compns. designed to prevent **neuronal cell death.**

IT **177159-38-5**, VLGGGSALLRSIPA **177718-96-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective and neurotrophic peptides from activity dependent neurotrophic factor)

L3 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 30 May 1996
ACCESSION NUMBER: 1996:314250 CAPLUS
DOCUMENT NUMBER: 125:1603
TITLE: A femtomolar-acting neuroprotective peptide
AUTHOR(S): Brenneman, Douglas E.; Gozes, Illana
CORPORATE SOURCE: Natl. Institute Child Health and Human Development, Natl. Institutes Health, Bethesda, MD, 20892-4480, USA
SOURCE: Journal of Clinical Investigation (1996), 97(10), 2299-2307
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel 14-amino acid peptide, with stress-protein-like sequences, exhibiting neuroprotection at unprecedented concns., is revealed. This peptide prevented **neuronal cell death** associated with the envelope protein (GP 120) from HIV, with excitotoxicity (NMDA), with the beta amyloid peptide (putative cytotoxin in Alzheimer's disease), and with tetrodotoxin (elec. blockade). The peptide was designed to contain a sequence derived from a new neuroprotective protein secreted by astroglial cells in the presence of vasoactive intestinal peptide. The neurotrophic protein was isolated by sequential chromatog. methods combining ion exchange, size separation, and hydrophobic interaction.

The protein (mol. mass, 14 kDa and pI, 8.3) was named activity-dependent neurotrophic factor, as it protected neurons from death associated with elec. blockade. Peptide sequencing led to the synthesis of the novel 14-amino acid peptide that was homologous, but not identical, to an intracellular stress protein, heat shock protein 60. Neutralizing antiserum to heat shock protein 60 produced **neuronal cell death** that could be prevented by cotreatment with the novel protein, suggesting the existence of extracellular stress-like proteins with neuroprotective properties. These studies identify a potent neuroprotective glial protein and an active peptide that provide a basis for developing treatments of

currently intractable neurodegenerative diseases.
IT **177159-38-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective peptide from activity-dependent neurotrophic factor acts at femtomolar levels)

E1 THROUGH E33 ASSIGNED

FILE 'REGISTRY' ENTERED AT 10:38:12 ON 24 FEB 2005
L4 33 SEA FILE=REGISTRY ABB=ON PLU=ON (177718-96-6/BI OR 211439-12-2/BI OR 177159-38-5/BI OR 211439-10-0/BI OR 209051-20-7/BI OR 209051-27-4/BI OR 292039-06-6/BI OR 292039-07-7/BI OR 292039-08-8/BI OR 327157-61-9/BI OR 327157-62-0/BI OR 211681-43-5/BI OR 211681-48-0/BI OR 270084-37-2/BI OR 270084-38-3/BI OR 292039-03-3/BI OR 292039-04-4/BI OR 292039-05-5/BI OR 188781-55-7/BI OR 223533-74-2/BI OR 270898-03-8/BI OR 270898-05-0/BI OR 320609-76-5/BI OR 327157-63-1/BI OR 590465-44-4/BI OR 590465-45-5/BI OR 590465-46-6/BI OR 590465-47-7/BI OR 590465-48-8/BI OR 590465-49-9/BI OR 590516-42-0/BI OR 590516-43-1/BI OR 590516-45-3/BI)

L5 33 L1 AND L4

L5 ANSWER 1 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **590516-45-3** REGISTRY
CN 26: PN: US6613740 SEQID: 41 unclaimed protein (9CI) (CA INDEX NAME)
CI MAN
SQL 800

SEQ
1 MVNRLSIPKP NLNSTGVNMM SSVHLQQNNY GVKSVGQGYS VGQSMRLGLG
51 GNAPVSIPQQ SQSVKQLLPS GNGRSYGLGS EQRSQAPARY SLQSANASSL
========
101 SSGHLKSPSL SHSQASRVLG QSSSKPAAAA TGPPPGNTSS TQKWKICTIC
151 NELFPENVYS VHFEKEHKAE KVPAVANYIM KIHNFTSKCL YCNRYLPTDT
201 LLNHMLIHGL SCPYCRSTFN DVEKMAAHMR MVHIDEEMGP KTDSTLSFDL
251 TLQQGSHTNI HLLVTTYNLR DAPAESVAYH AQNNPPVPPK PQPKVQEKAD
301 IPVKSSPQAA VPYKKDVGKT LCPLCFSILK GPISDALAHH LRERHQVIQT
351 VHPVEKKLTY KCIHCLGVYT SNMTASTITL HLVHCRGVGK TQNGQDKTNA
401 PSRLNQSPSL APVKRTYEQM EFPLLKKRKL DDDSDSPSFF EEKPEEPVVL
451 ALDPKGHEDD SYEARKSFLT KYFNKQPYPT RREIEKLAAS LWLWKSDIAS
501 HFSNKRKKCV RDCEKYKPGV LLGFNMKELN KVKHEMDFDA EWLFENHDEK
551 DSRVNASKTA DKKLNLGKED DSSSDSFENL EEESNESGSP FDPVFEVEPK
601 ISNDNPEEHV LKVIPEDASE SEEKLDQKED GSKYETIHLT EEPTKLMHNA
651 SDSEVDQDDV VEWKDGASPS ESGPGSQQVS DFEDNTCEMK PGTWSDESSQ
701 SEDARSSKPA AKKKATMQGD REQLKWKNSS YGKVEGFWSK DQSQWKNASE
751 NDERLSNPQI EWQNSTIDSE DGEQFDNMTD GVTEPMHGSL AGVKLSSQQA
HITS AT: 52-59

REFERENCE 1: 139:208245

L5 ANSWER 2 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **590516-43-1** REGISTRY
CN 24: PN: US6613740 SEQID: 32 unclaimed protein (9CI) (CA INDEX NAME)
CI MAN
SQL 781

SEQ
1 MSSVHLQQNN YGVKSVGQGY SVGQSMRLGL GGNAPVSIPQ QSQSVKQLLP

```
                                                    ========
        51 SGNGRSYGLG SEQRSQAPAR YSLQSANASS LSSGHLKSPS LSHSQASRVL
       101 GQSSSKPAAA ATGPPPGNTS STQKWKICTI CNELFPENVY SVHFEKEHKA
       151 EKVPAVANYI MKIHNFTSKC LYCNRYLPTD TLLNHMLIHG LSCPYCRSTF
       201 NDVEKMAAHM RMVHIDEEMG PKTDSTLSFD LTLQQGSHTN IHLLVTTYNL
       251 RDAPAESVAY HAQNNPPVPP KPQPKVQEKA DIPVKSSPQA AVPYKKDVGK
       301 TLCPLCFSIL KGPISDALAH HLRERHQVIQ TVHPVEKKLT YKCIHCLGVY
       351 TSNMTASTIT LHLVHCRGVG KTQNGQDKTN APSRLNQSPS LAPVKRTYEQ
       401 MEFPLLKKRK LDDDSDSPSF FEEKPEEPVV LALDPKGHED DSYEARKSFL
       451 TKYFNKQPYP TRREIEKLAA SLWLWKSDIA SHFSNKRKKC VRDCEKYKPG
       501 VLLGFNMKEL NKVKHEMDFD AEWLFENHDE KDSRVNASKT ADKKLNLGKE
       551 DDSSSDSFEN LEEESNESGS PFDPVFEVEP KISNDNPEEH VLKVIPEDAS
       601 ESEEKLDQKE DGSKYETIHL TEEPTKLMHN ASDSEVDQDD VVEWKDGASP
       651 SESGPGSQQV SDFEDNTCEM KPGTWSDESS QSEDARSSKP AAKKKATMQG
       701 DREQLKWKNS SYGKVEGFWS KDQSQWKNAS ENDERLSNPQ IEWQNSTIDS
       751 EDGEQFDNMT DGVTEPMHGS LAGVKLSSQQ A
HITS AT:    33-40

REFERENCE   1:  139:208245

L5   ANSWER 3 OF 33  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   590516-42-0  REGISTRY
CN   23: PN: US6613740 SEQID: 31 unclaimed protein (9CI)  (CA INDEX NAME)
CI   MAN
SQL  787

SEQ      1 MSNVHLQQNN YGVKSVGQSY GVGQSVRLGL GGNAPVSIPQ QSQSVKQLLP
                                                    ========
        51 SGNGRSFGLG AEQRPPAAAR YSLQTANTSL PPGQVKSPSV SQSQASRVLG
       101 QSSSKPPPAA TGPPPSNHCA TQKWKICTIC NELFPENVYS VHFEKEHKAE
       151 KVPAVANYIM KIHNFTSKCL YCNRYLPTDT LLNHMLIHGL SCPYCRSTFN
       201 DVEKMAAHMR MVHIDEEMGP KTDSTLSFDL TLQQGSHTNI HLLVTTYNLR
       251 DAPAESVAYH AQNNAPVPPK PQPKVQEKAD VPVKSSPQAA VPYKKDVGKT
       301 LCPLCFSILK GPISDALAHH LRERHQVIQT VHPVEKKLTY KCIHCLGVYT
       351 SNMTASTITL HLVHCRGVGK TQNGQDKTNA PSRLNQSPGL APVKRTYEQM
       401 EFPLLKKRKL EEDADSPSCF EEKPEEPVVL ALDPKGHEDD SYEARKSFLT
       451 KYFNKQPYPT RREIEKLAAS LWLWKSDIAS HFSNKRKKCV RDCEKYKPGV
       501 LLGFNMKELN KVKHEMDFDA EWLFENHDEK DSRVNASKTV DKKHNLGKED
       551 DSFSDSFEHL EEESNGSGSP FDPVFEVEPK IPSDNLEEPV PKVIPEGALE
       601 SEKLDQKEEE EEEEEEDGSK YETIHLTEEP AKLMHDASDS EVDQDDVVEW
       651 KDGASPSESG PGSQQISDFE DNTCEMKPGT WSDESSQSED ARSSKPAAKK
       701 KATVQDDTEQ LKWKNSSYGK VEGFWSKDQS QWENASENAE RLPNPQIEWQ
       751 NSTIDSEDGE QFDSMTDGVA DPMHGSLTGV KLSSQQA
HITS AT:    33-40

REFERENCE   1:  139:208245

L5   ANSWER 4 OF 33  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   590465-49-9  REGISTRY
CN   Activity-dependent neurotrophic factor III (Mus musculus 828-amino acid
     isoform) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   29: PN: US6613740 SEQID: 55 claimed protein
CI   MAN
SQL  828
```

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SEQ      1 MGLPPRISSL ASGNVRSLPS QQMVNRLSIP KPNLNSTGVN MMSNVHLQQN
        51 NYGVKSVGQS YGVGQSVRLG LGGNAPVSIP QQSQSVKQLL PSGNGRSFGL
                                   ======= =
       101 GAEQRPPAAA RYSLQTANTS LPPGQVKSPS VSQSQASRVL GQSSSKPPPA
       151 ATGPPPSNHC ATQKWKICTI CNELFPENVY SVHFEKEHKA EKVPAVANYI
       201 MKIHNFTSKC LYCNRYLPTD TLLNHMLIHG LSCPYCRSTF NDVEKMAAHM
       251 RMVHIDEEMG PKTDSTLSFD LTLQQGSHTN IHLLVTTYNL RDAPAESVAY
       301 HAQNNAPVPP KPQPKVQEKA DVPVKSSPQA AVPYKKDVGK TLCPLCFSIL
       351 KGPISDALAH HLRERHQVIQ TVHPVEKKLT YKCIHCLGVY TSNMTASTIT
       401 LHLVHCRGVG KTQNGQDKTN APSRLNQSPG LAPVKRTYEQ MEFPLLKKRK
       451 LEEDADSPSC FEEKPEEPVV LALDPKGHED DSYEARKSFL TKYFNKQPYP
       501 TRREIEKLAA SLWLWKSDIA SHFSNKRKKC VRDCEKYKPG VLLGFNMKEL
       551 NKVKHEMDFD AEWLFENHDE KDSRVNASKT VDKKHNLGKE DDSFSDSFEH
       601 LEEESNGSGS PFDPVFEVEP KIPSDNLEEP VPKVIPEGAL ESEKLDQKEE
       651 EEEEEEEDGS KYETIHLTEE PAKLMHDASD SEVDQDDVVE WKDGASPSES
       701 GPGSQQISDF EDNTCEMKPG TWSDESSQSE DARSSKPAAK KKATVQDDTE
       751 QLKWKNSSYG KVEGFWSKDQ SQWENASENA ERLPNPQIEW QNSTIDSEDG
       801 EHFDSMTDGV ADPMHGSLTG VKLSSQQA
HITS AT:    74-81

REFERENCE   1:  139:208245

L5   ANSWER 5 OF 33  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   590465-48-8  REGISTRY
CN   Activity-dependent neurotrophic factor III (Mus musculus 806-amino acid
     isoform) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   10: PN: US6613740 SEQID: 3 claimed protein
CI   MAN
SQL  806

SEQ      1 MVNRLSIPKP NLNSTGVNMM SNVHLQQNNY GVKSVGQSYG VGQSVRLGLG
        51 GNAPVSIPQQ SQSVKQLLPS GNGRSFGLGA EQRPPAAARY SLQTANTSLP
           ========
       101 PGQVKSPSVS QSQASRVLGQ SSSKPPPAAT GPPPSNHCAT QKWKICTICN
       151 ELFPENVYSV HFEKEHKAEK VPAVANYIMK IHNFTSKCLY CNRYLPTDTL
       201 LNHMLIHGLS CPYCRSTFND VEKMAAHMRM VHIDEEMGPK TDSTLSFDLT
       251 LQQGSHTNIH LLVTTYNLRD APAESVAYHA QNNAPVPPKP QPKVQEKADV
       301 PVKSSPQAAV PYKKDVGKTL CPLCFSILKG PISDALAHHL RERHQVIQTV
       351 HPVEKKLTYK CIHCLGVYTS NMTASTITLH LVHCRGVGKT QNGQDKTNAP
       401 SRLNQSPGLA PVKRTYEQME FPLLKKRKLE EDADSPSCFE EKPEEPVVLA
       451 LDPKGHEDDS YEARKSFLTK YFNKQPYPTR REIEKLAASL WLWKSDIASH
       501 FSNKRKKCVR DCEKYKPGVL LGFNMKELNK VKHEMDFDAE WLFENHDEKD
       551 SRVNASKTVD KKHNLGKEDD SFSDSFEHLE EESNGSGSPF DPVFEVEPKI
       601 PSDNLEEPVP KVIPEGALES EKLDQKEEEE EEEEEDGSKY ETIHLTEEPA
       651 KLMHDASDSE VDQDDVVEWK DGASPSESGP GSQQISDFED NTCEMKPGTW
       701 SDESSQSEDA RSSKPAAKKK ATVQDDTEQL KWKNSSYGKV EGFWSKDQSQ
       751 WENASENAER LPNPQIEWQN STIDSEDGEQ FDSMTDGVAD PMHGSLTGVK
       801 LSSQQA
HITS AT:    52-59

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE   1:  139:208245

L5   ANSWER 6 OF 33  REGISTRY  COPYRIGHT 2005 ACS on STN
```

RN **590465-47-7** REGISTRY
CN Activity-dependent neurotrophic factor III (human clone H7) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 33: PN: US6613740 SEQID: 59 claimed protein
CI MAN
SQL 874

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SEQ      1 MPKSYEALVQ HVIEDHERIG YQVTAMIGHT NVVVPRSKPL MLIAPKPQDK
        51 KSMGLPPRIG SLASGNVRSL PSQQMVNRLS IPKPNLNSTG VNMMSSVHLQ
       101 QNNYGVKSVG QGYSVGQSMR LGLGGNAPVS IPQQSQSVKQ LLPSGNGRSY
                                   ===== ===
       151 GLGSEQRSQA PARYSLQSAN ASSLSSGQLK SPSLSQSQAS RVLGQSSSKP
       201 AAAATGPPPG NTSSTQKWKI CTICNELFPE NVYSVHFEKE HKAEKVPAVA
       251 NYIMKIHNFT SKCLYCNRYL PTDTLLNHML IHGLSCPYCR STFNDVEKMA
       301 AHMRMVHIDE EMGPKTDSTL SFDLTLQQGS HTNIHLLVTT YNLRDAPAES
       351 VAYHAQNNPP VPPKPQPKVQ EKADIPVKSS PQAAVPYKKD VGKTLCPLCF
       401 SILKGPISDA LAHHLRERHQ VIQTVHPVEK KLTYKCIHCL GVYTSNMTAS
       451 TITLHLVHCR GVGKTQNGQD KTNAPSRLNQ SPSLAPVKRT YEQMEFPLLK
       501 KRKLDDDSDS PSFFEEKPEE PVVLALDPKG HEDDSYEARK SFLTKYFNKQ
       551 PYPTRREIEK LAASLWLWKS DIASHFSNKR KKCVRDCEKY KPGVLLGFNM
       601 KELNKVKHEM DFDAEWLFEN HDEKDSRVNA SKTADKKLNL GKEDDSSSDS
       651 FENLEEESNE SGSPFDPVFE VEPKISNDNP EEHVLKVIPE DASESEEKLD
       701 QKEDGSKYET IHLTEEPTKL MHNASDSEVD QDDVVEWKDG ASPSESGPGS
       751 QQVSDFEDNT CEMKPGTWSD ESSQSEDARS SKPAAKKKAT MQGDREQLKW
       801 KNSSYGKVEG FWSKDQSQWK NASENDERLS NPQIEWQNST IDSEDGEQFD
       851 NMTDGVAEPM HGSLAGVKLS SQQA
HITS AT:   126-133
```

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 139:208245

L5 ANSWER 7 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **590465-46-6** REGISTRY
CN Activity-dependent neurotrophic factor III (human clone H3) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 31: PN: US6613740 SEQID: 57 claimed protein
CI MAN
SQL 726

```
SEQ      1 RSLPSQQMVN RLSIPKPNLN STGVNMMSSV HLQQNNYGVK SVGQGYSVGQ
        51 SMRLGLGGNA PVSIPQQSQS VKQLLPSGNG RSYGLGSEQR SQAPARYSLQ
                   == ======
       101 SANASSLSSG QLKSPSLSQS QASRVLGQSS SKPAAAATGP PPGNTSSTQK
       151 WKICTICNEL FPENVYSVHF EKEHKAEKVP AVANYIMKIH NFTSKCLYCN
       201 RYLPTDTLLN HMLIHGLSCP YCRSTFNDVE KMAAHMRMVH IDEEMGPKTD
       251 STLSFDLTLQ QGSHTNIHLL VTTYNLRDAP AESVAYHAQN NPPVPPKPQP
       301 KVQEKADIPV KSSPQAAVPY KKDVGKTLCP LCFSILKGPI SDALAHHLRE
       351 RHQVIQTVHP VEKKLTYKCI HCLGVYTSNM TASTITLHLV HCRGVGKTQN
       401 GQDKTNAPSR LNQSPSLAPV KRTYEQMEFP LLKKRKLDDD SDSPSFFEEK
       451 PEEPVVLALD PKGHEDDSYE ARKSFLTKYF NKQPYPTRRE IEKLAASLWL
       501 WKSDIASHFS NKRKKCVRDC EKYKPGVLLG FNMKELNKVK HEMDFDAEWL
       551 FENHDEKDSR VNASKTADKK LNLGKEDDSS SDSFENLEEE SNESGSPFDP
       601 VFEVEPKISN DNPEEHVLKV IPEDASESEE KLDQKEDGSK YETIHLTEEP
```

651 TKLMHNASDS EVDQDDVVEW KDGASPSESG PGSQQVSDFE DNTCEMKPGT
701 WSDESSQSED ARSSKPAAKK KGYHAR
HITS AT: 59-66

REFERENCE 1: 139:208245

L5 ANSWER 8 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **590465-45-5** REGISTRY
CN Activity-dependent neurotrophic factor III (human clone H3') (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 8: PN: US6613740 SEQID: 1 claimed protein
CI MAN
SQL 1000

SEQ 1 MVNRLSIPKP NLNSTGVNMM SSVHLQQNNY GVKSVGQGYS VGQSMRLGLG
51 GNAPVSIPQQ SQSVKQLLPS GNGRSYGLGS EQRSQAPARY SLQSANASSL
========
101 SSGHLKSPSL SHSQASRVLG QSSSKPAAAA TGPPPGNTSS TQKWKICTIC
151 NELFPENVYS VHFEKEHKAE KVPAVANYIM KIHNFTSKCL YCNRYLPTDT
201 LLNHMLIHGL SCPYCRSTFN DVEKMAAHMR MVHIDEEMGP KTDSTLSFDL
251 TLQQGSHTNI HLLVTTYNLR DAPAESVAYH AQNNPPVPPK PQPKVQEKAD
301 IPVKSSPQAA VPYKKDVGKT LCPLCFSILK GPISDALAHH LRERHQVIQT
351 VHPVEKKLTY KCIHCLGVYT SNMTASTITL HLVHCRGVGK TQNGQDKTNA
401 PSRLNQSPSL APVKRTYEQM EFPLLKKRKL DDDSDSPSFF EEKPEEPVVL
451 ALDPKGHEDD SYEARKSFLT KYFNKQPYPT RREIEKLAAS LWLWKSDIAS
501 HFSNKRKKCV RDCEKYKPGV LLGFNMKELN KVKHEMDFDA EWLFENHDEK
551 DSRVNASKTA DKKLNLGKED DSSSDSFENL EEESNESGSP FDPVFEVEPK
601 ISNDNPEEHV LKVIPEDASE SEEKLDQKED GSKYETIHLT EEPTKLMHNA
651 SDSEVDQDDV VEWKDGASPS ESGPGSQQVS DFEDNTCEMK PGTWSDESSQ
701 SEDARSSKPA AKKKATMQGD REQLKWKNSS YGKVEGFWSK DQSQWKNASE
751 NDERLSNPQI EWQNSTIDSE DGEQFDNMTD GVTEPMHGSL AGVKLSSQQA
801 XVPGSLALVT CCSLELXSPV XLQSCLLTGT ALXVLVGLWG MWPLQFQWLF
851 LSLXQDRLFL LQNLLXQTRX LNVKNQXAGD SXILTRKSRG LFLSAFSTFL
901 SLCEMIGQMS LRSVKLIHMV VXGQHTSYQS NVYSRLWEKR FFFMYSFXIV
951 EMYICTVFXT YSKXCSXSCY CVPIIDFFFX CCPCCVINAL SSLPSKSSKL
HITS AT: 52-59

REFERENCE 1: 139:208245

L5 ANSWER 9 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **590465-44-4** REGISTRY
CN 15: PN: US6613740 SEQID: 10 claimed protein (9CI) (CA INDEX NAME)
CI MAN
SQL 88

SEQ 1 XXXXXXXXXX XXXXXXXXXX XXXXXXXXXX XXXXXXXXXX NAPVSIPQXX
========
51 XXXXXXXXXX XXXXXXXXXX XXXXXXXXXX XXXXXXXX
HITS AT: 41-48

REFERENCE 1: 139:208245

L5 ANSWER 10 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **327157-63-1** REGISTRY
CN D-Glutamine, D-asparaginyl-D-alanyl-L-prolyl-D-valyl-D-seryl-D-isoleucyl-D-

prolyl- (9CI) (CA INDEX NAME)
SQL 8

SEQ 1 NAPVSIPQ
========
HITS AT: 1-8

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 134:198025

L5 ANSWER 11 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **327157-62-0** REGISTRY
CN D-Glutamine, D-asparaginyl-D-alanyl-D-prolyl-D-valyl-D-seryl-D-isoleucyl-D-prolyl- (9CI) (CA INDEX NAME)
CI COM
SQL 8

SEQ 1 NAPVSIPQ
========
HITS AT: 1-8

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 141:201591

REFERENCE 2: 141:64409

REFERENCE 3: 136:1116

REFERENCE 4: 134:198025

L5 ANSWER 12 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **327157-61-9** REGISTRY
CN D-Alanine, D-seryl-D-alanyl-D-leucyl-D-leucyl-D-arginyl-D-seryl-D-isoleucyl-D-prolyl- (9CI) (CA INDEX NAME)
CI COM
SQL 9

SEQ 1 SALLRSIPA
=========
HITS AT: 1-9

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 141:201591

REFERENCE 2: 141:64409

REFERENCE 3: 136:1116

REFERENCE 4: 134:198025

L5 ANSWER 13 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **320609-76-5** REGISTRY
CN Peptide, (Xaa-Ser-Ala-Leu-Leu-Arg-Ser-Ile-Pro-Ala-Xaa) (9CI) (CA INDEX

NAME)
OTHER NAMES:
CN 1: PN: US6174862 SEQID: 16 claimed protein
CI MAN
SQL 11

SEQ 1 XSALLRSIPA X
=========
HITS AT: 2-10

REFERENCE 1: 134:120910

L5 ANSWER 14 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **292039-08-8** REGISTRY
CN L-Serine, L-leucylglycyl-L-leucylglycylglycyl-L-asparaginyl-L-alanyl-L-prolyl-L-valyl-L-seryl-L-isoleucyl-L-prolyl-L-glutaminyl-L-glutaminyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 18: PN: US6613740 SEQID: 35 unclaimed protein
CN 23: PN: WO2004080957 SEQID: 11 claimed sequence
CN 7: PN: WO2004060309 SEQID: 4 claimed protein
SQL 15

SEQ 1 LGLGGNAPVS IPQQS
===== ===
HITS AT: 6-13

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 139:208245

REFERENCE 4: 136:1116

REFERENCE 5: 134:198025

REFERENCE 6: 133:233267

L5 ANSWER 15 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **292039-07-7** REGISTRY
CN L-Serine, L-leucylglycylglycyl-L-asparaginyl-L-alanyl-L-prolyl-L-valyl-L-seryl-L-isoleucyl-L-prolyl-L-glutaminyl-L-glutaminyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 17: PN: US6613740 SEQID: 34 unclaimed protein
CN 22: PN: WO2004080957 SEQID: 10 claimed sequence
CN 6: PN: WO2004060309 SEQID: 3 claimed protein
SQL 13

SEQ 1 LGGNAPVSIP QQS
======= =
HITS AT: 4-11

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 139:208245

REFERENCE 4: 136:1116

REFERENCE 5: 134:198025

REFERENCE 6: 133:233267

L5 ANSWER 16 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **292039-06-6** REGISTRY
CN L-Glutamine, glycylglycyl-L-asparaginyl-L-alanyl-L-prolyl-L-valyl-L-seryl-L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 10: PN: WO2004060309 SEQID: 20 claimed protein
CN 16: PN: US6613740 SEQID: 33 unclaimed protein
CN 21: PN: WO2004080957 SEQID: 9 claimed sequence
SQL 10

SEQ 1 GGNAPVSIPQ
========
HITS AT: 3-10

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 139:208245

REFERENCE 4: 136:1116

REFERENCE 5: 134:198025

REFERENCE 6: 133:233267

L5 ANSWER 17 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **292039-05-5** REGISTRY
CN L-Alanine, glycylglycyl-L-seryl-L-alanyl-L-leucyl-L-leucyl-L-arginyl-L-seryl-L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 19: PN: WO2004080957 SEQID: 7 claimed sequence
CN 4: PN: WO2004060309 SEQID: 18 claimed protein
SQL 11

SEQ 1 GGSALLRSIP A
======== =
HITS AT: 3-11

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 136:1116

REFERENCE 4: 134:198025

REFERENCE 5: 133:233267

L5 ANSWER 18 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **292039-04-4** REGISTRY
CN L-Alanine, glycylglycylglycyl-L-seryl-L-alanyl-L-leucyl-L-leucyl-L-arginyl-L-seryl-L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 18: PN: WO2004080957 SEQID: 6 claimed sequence
CN 3: PN: WO2004060309 SEQID: 17 claimed protein
SQL 12

SEQ 1 GGGSALLRSI PA
=======
HITS AT: 4-12

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 136:1116

REFERENCE 4: 134:198025

REFERENCE 5: 133:233267

L5 ANSWER 19 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **292039-03-3** REGISTRY
CN L-Alanine, L-leucylglycylglycylglycyl-L-seryl-L-alanyl-L-leucyl-L-leucyl-L-arginyl-L-seryl-L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 17: PN: WO2004080957 SEQID: 5 claimed sequence
CN 2: PN: WO2004060309 SEQID: 16 claimed protein
SQL 13

SEQ 1 LGGGSALLRS IPA
======
HITS AT: 5-13

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 136:1116

REFERENCE 4: 134:198025

REFERENCE 5: 133:233267

L5 ANSWER 20 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **270898-05-0** REGISTRY
CN 32: PN: WO0027875 FIGURE: 13 unclaimed sequence (9CI) (CA INDEX NAME)
CI MAN
SQL 874

SEQ 1 MPKSYEALVQ HVIEDHERIG YQVTAMIGHT NVVVPRSKPL MLIAPKPQDK